



## Evidence-Based Laboratory Medicine (EBLM) in autoimmunity

The diagnosis of autoimmune diseases is based on clinical and instrumental data, as well as on laboratory investigations. This aspect has become increasingly important as immunological techniques have progressively improved thanks to two prevailing components: the advancement of analytical technologies and the evolution of knowledge on the molecular basis of antigens targeted by autoantibodies [1].

This remarkable development of immunological diagnostics has meant that the search for serum autoantibodies has wider implications, i.e. not only for diagnosing autoimmune diseases but also for prognostic evaluation and therapeutic monitoring [2]. Therefore, the contribution of laboratory medicine to improving health care is in providing evidence that laboratory test results are clinically relevant and that high quality laboratory tests contribute to correct and timely clinical decisions [3–6]. However, this breakthrough brings the need to choose from available technological and organizational solutions, seeking the most effective in simultaneously achieving accurate information and cost containment.

To this end, over the past 20 years, Evidence-Based Medicine (EBM) proved to be a scientifically validated and objective tool, to find the best available evidence to help make better choices. EBM is the conscientious, explicit and judicious use of current best evidence in making decision about the care of individual patients [7]. This definition of EBM by David Sackett specifically includes pathology and diagnostic tests, because these are important parts of the decision-making process [8]. From a practical point of view, EBM means integrating individual clinical expertise with the best available scientific evidence; while identifying the best evidence means using epidemiological and biostatistical tools for a critical appraisal of evidence, such as systematic reviews. In this context, systematic means a synthesis of all the information available, avoiding those which have been known sources of bias. Thus, systematic reviews should be as scientific and rigorous as the articles they review. Indeed, one of the goals of systematic reviews and meta-analysis is to reduce or eliminate bias, preventing wrong results from individual studies.

The Study Group on Autoimmunology of the Italian Society of Laboratory Medicine (SIMeL) has addressed these issues in a recent meeting held in Paestum, Italy, on May 7–9, 2011. The goal was to provide clearly expressed, understandable examples of the value of laboratory testing, through systematic reviews on some relevant autoantibody tests for the diagnosis of autoimmune diseases.

Evidence on the relationship between infectious agents and autoimmune diseases was the subject of the introductory lecture by Prof. Yehuda Shoenfeld, which covered the most important aspects of the complicated causal interaction between infectious diseases and autoimmune diseases.

Issues relating to procedures and methods of statistical analysis on how to perform a systematic review and a meta-analysis were addressed by Davide Giavarina [9]. His presentation focused on the fact that understanding diagnostic test accuracy from different study results can help improve critical appraisal of evidence about the best use of diagnostic tests.

Subsequent reports were the result of collaborative systematic reviews and meta-analyses of literature data on some areas of diagnostic interest in autoimmune diseases.

The meaning and diagnostic role of anti-nucleosome antibodies were the objects of the study performed by Nicola Bizzaro et al. [10]. This systematic review analyzed the diagnostic and prognostic value of these antibodies and, in particular, the behavior of anti-nucleosome antibodies compared to anti-dsDNA antibodies. Data from the meta-analysis have shown that anti-nucleosome antibodies have equal specificity but higher sensitivity and prognostic value than anti-dsDNA antibodies in the diagnosis of systemic lupus erythematosus and that, despite a certain heterogeneity among the various studies, the use of anti-nucleosome antibody test appears more efficacious than anti-dsDNA testing.

Renato Tozzoli et al. have analyzed the diagnostic performance of tests for the measurement of anti-TSH receptor antibodies (TRAb), evaluating the indices of diagnostic accuracy of the 1st, 2nd and 3rd generation immunoassay methods [11]. Data from the meta-analysis have shown that TRAb measured with the 2nd and 3rd generation methods have very high sensitivity and specificity in the diagnosis of Graves' disease. The differences between the 2nd and 3rd generation methods are small and they are equally useful. One important finding derived from this study is that, in contrast with recommendations made by clinical endocrinologists, widespread use of this test is highly effective to screen hyperthyroid patients. The evidence provided by this meta-analysis should prompt appropriate revision of the current guidelines.

The diagnostic accuracy of commercially available enzyme-linked immunosorbent assays (ELISA) to detect anti-BP180, anti-BP230 and anti-desmoglein 3 autoantibodies in the diagnosis of autoimmune blistering skin diseases, has been investigated by Marilina Tampoia et al. [12]. Results of this systematic review show that anti-BP180 and anti-desmoglein 3 autoantibodies are very accurate to diagnose pemphigus and pemphigoid, while anti-BP230 antibodies lack sensitivity.

Daniilo Villalta et al. have looked for evidence in the literature with an updated review on the diagnostic systems for detecting antibodies in systemic sclerosis (SSc) [13]. The aim of this study was to evaluate the diagnostic accuracy and the clinical association of 13 different SSc-associated autoantibodies.

Finally, a topic of great relevance, the systematic review conducted by Antonio Antico et al. [14] evaluated whether vitamin D levels are related to the risk of developing autoimmune diseases and whether supplementation with vitamin D can modify the course of the diseases.

We are grateful to Prof. Shoenfeld, Editor of Autoimmunity Reviews, for his invitation to publish the results of these studies in a special issue of the Journal. We hope that they can be useful both to those who are called to choose among the different methods offered by the biomedical industry, and to clinicians whose task is to translate these data into concrete actions and effective patient care.

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